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Environmental
Protection Agency

Office of Pollution
Prevention and Toxics
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Pollution Prevention

(P2) Framework

U.S. Environmental Protection Agency

Office of Pollution Prevention and Toxics

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Disclaimers

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The models presented in OPPT's P2 Framework have been developed over a period of more than 20 years by OPPT, EPA contractors and/or grantees or others in the scientific and technical community, to screen chemicals in the absence of data. Through the P2 Framework, OPPT is presenting these screening models to industry and other stakeholders in the hopes that use of these models early in the research and development process will result in safer chemicals entering commerce. The P2 Framework models should be used to provide additional information on chemicals of concern.

Other chemical screening methodologies have been developed and are in use by chemical companies and other stakeholders. The Agency recognizes that other models are available and that these models can also be of value in chemical screening efforts.

CAUTION: Screening models provide estimations with an inherent degree of uncertainty, and should *never* be used to replace measured data from well designed studies. Measured data are always preferred over predicted data. If measured data are not available, measured data on close analogs can be used. If no analog data are available, screening level models, such as those in the P2 Framework, may be used to predict values that can be used to indicate which chemicals may need further testing.

NOTE: The URLs of certain Internet sites are provided as a convenience to users of the manual. Users are cautioned that due to the dynamic nature of the Internet, these URLs may have been changed from the time of the writing of this document. In case a URL is no longer correct, the user is advised to use any of the search engines to locate the correct URL.

NOTE: This document can be downloaded in PDF format from the Internet at
http://www.epa.gov/oppt/p2framework/docs/p2manua.htm

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Executive Summary

Publicly Available Data to Predict Chemical Risk are Often Lacking

Of the approximately 80,000 chemicals used in commerce in the United States, few have been tested, and only a fraction have sufficient publicly available data to allow a thorough evaluation of risk. Businesses, governmental organizations, and other stakeholders often don't have the data necessary to identify problem chemicals or identify safer substitutes or other options that are less risky, prevent pollution, and may save companies environmental management costs. At times, companies must make product and process decisions without enough data regarding the risk tradeoffs.

OPPT Screening Methods to Predict Risk-Related Information

The Office of Pollution Prevention and Toxics (OPPT) has developed computer-based methods that derive important risk assessment information based on chemical structure, conservative defaults, standard scenarios, and other factors. These methods provide information on physical / chemical properties, environmental fate, potential carcinogenicity, toxicity to aquatic organisms, worker and general population exposures, among other data. OPPT routinely uses these methods to highlight chemicals of concern, to identify safer substitutes, and to reduce or eliminate risks.

P2 Framework – a Compilation of OPPT Screening Methods

The Pollution Prevention Framework ("P2 Framework") is compilation of many of OPPT's most important computer-based methods for predicting risk-related information. The P2 Framework provides important methods to predict risk-related information that may not be readily available. Its purpose is to provide information that can inform decision making and help promote the design, development, and application of safer chemicals, products, and processes. The document describes each methodology and the importance of the data generated, and provides case studies showing how methods can be used collectively to answer complicated risk assessment questions and identify pollution prevention opportunities. The P2 Framework, as currently constructed, does not address all biological endpoints. It is a set of screening-level methods that are of most value when chemical-specific data are lacking.

Sustainable Futures Initiative

Sustainable Futures is the programmatic structure OPPT developed to scale-up the successful P2 Framework-based Kodak and PPG Project XLs, and is designed to help industry develop new chemicals that are sustainable economically and environmentally. OPPT published a Federal Register notice announcing Sustainable Futures on December 11, 2002. The FR Notice is available at www.epa.gov/fedrgstr/EPA-TOX/2002/December/Day-11/t31243.pdf. Sustainable Futures offers industry an integrated path to the development of safer chemicals. This path includes: (1) comprehensive training in the use of the P2 Framework models, (2) specialized technical assistance within each industry sector, and (3) a Small Business Assistance Program, and (4) strong incentives.

Incentives

OPPT is offering regulatory flexibility to companies that participate in Sustainable Futures, allowing qualifying chemicals to be manufactured in 45 days, rather than the current 90-day structure. This is a powerful incentive for many companies. In addition to getting to market sooner, regulatory uncertainty is greatly reduced because the P2 Framework helps anticipate, and engineer away from, chemicals of concern. This is P2 in it purest form. In addition, use of the P2 Framework reduces product development and manufacturing costs.

Pollution Prevention and the Risk Assessment Process

What Is Pollution Prevention (P2)?

"Pollution Prevention", or "P2" is the common sense understanding that it is easier to prevent problems than to correct them. Congress, by enacting the Pollution Prevention Act of 1990 (42 U.S.C. 13101 and13102, s/s et seq.), created a bold national objective for environmental protection by outlining a hierarchy in dealing with pollution:

- Pollution should be prevented or reduced at the source whenever feasible;
- Pollution that cannot be prevented should be recycled in an environmentally safe manner whenever feasible;
- Pollution that cannot be prevented or recycled should be treated in an environmentally safe manner whenever feasible; and
- Disposal or other releases into the environment should be employed only as a last resort and should be conducted in an environmentally safe manner.

Pollution prevention means "source reduction," as defined under the Pollution Prevention Act. The Pollution Prevention Act defines "source reduction" to mean any practice which:

- Reduces the amount of any hazardous substance, pollutant, or contaminant entering any waste stream or otherwise released into the environment prior to recycling, treatment, or disposal; and
- Reduces the hazards to public health and the environment associated with the release of such substances, pollutants, or contaminants.

Source reduction can be achieved through equipment or technology modifications, processes or procedure modification, reformulation or redesign of products, substitution of materials, etc.

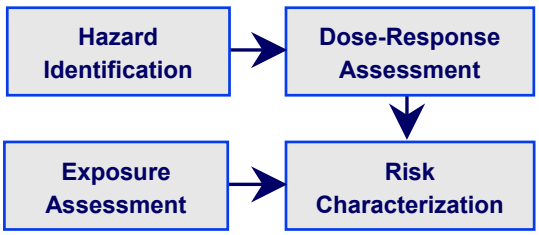
The Risk Assessment Process

In 1983, the National Academy of Sciences developed a 4 step paradigm for risk assessment and risk management*:

- **Hazard Identification**: Examining toxicity data to determine effects of a chemical on health of humans or other organisms (for example, increased cancer cases or birth defects);
- **Dose-Response Assessment**: Extrapolating toxicity data from high dose studies to predict the likely effect of low doses of the chemical (also referred to as Hazard Characterization);
- **Exposure Assessment**: Magnitude, frequency, and duration of exposure to a chemical (for example, exposures from proposed or actual manufacture, use, or disposal of a chemical); and
- **Risk Characterization**: Estimates potential for, and magnitude of, risk to an exposed individual or population.

The components of the risk assessment process are illustrated in the figure below.

The Risk Assessment Paradigm



*NRC. 1983. Risk Assessment in the Federal Government: Managing the Process. National Research Council. National Academy Press, Washington, DC. ISBN: 0-309-03349-7.

Risk Information Improves Decision Making

Understanding the Problem is Key to Identifying P2 Opportunities and Sustainability

Each year industry develops new chemical substances, substances previously unknown to commerce. The Toxic Substances Control Act (TSCA) gives EPA authority to regulate new chemicals, i.e., chemicals not already listed on the TSCA Inventory. For help determining if a chemical substance is on the TSCA Inventory go to http://www.epa.gov/opptintr/newchems/invntory.htm. EPA's regulatory authority to regulate new chemicals is described under the PreManufacture Notice (PMN) Provisions of TSCA. Before manufacture for commercial purposes, industry must submit a PMN to EPA, and EPA, OPPT has 90 days to identify chemicals posing risk(s) and regulate when needed. There is no requirement under TSCA that the submitter conduct testing on new chemicals, however if tests are conducted, this data must be submitted with the PMN. Less than 10% of PMNs submitted have publicly available data such as an LD50. An alarmingly small number of PMNs have enough publicly available data to perform a rudimentary assessment of risk.

Uncertain Risks

Industry submits 2,000 PMNs annually. In many cases, when alternative chemicals or processes are considered at R&D, commercialization decisions are based on factors such as efficacy, yield, performance, and cost. While EPA sees 2,000 PMNs per year, industry has made thousands of other decisions early in R&D, long before PMN submission. By the time EPA sees the PMN, most of the P2 opportunities have been lost. Industry has needed to make decisions without understanding risk tradeoffs of product/process alternatives.

Risk-Related Information is Needed to Take Advantage of P2 Opportunities

To identify and take advantage of pollution prevention opportunities, stakeholders need access to risk-related information. Companies often decide which chemicals or processes to use primarily on the basis of cost and product performance, among other criteria. If companies had access to risk-related information about chemicals, they could improve decision making and take advantage of pollution prevention opportunities.

Technology Provides an Opportunity

Faced with tight statutory deadlines (90 days) and the absence of hazard/risk data, OPPT turned to technology to fulfill its mission. Working with others in the scientific community, OPPT developed risk screening methods that use SARs - Structure Activity Relationships. The SAR approach calculates or infers hazard, exposure and risk issues based on an analysis of chemical structure. SAR techniques include computational toxicology, expert systems, among other approaches. Endpoints addressed include, environmental fate, cancer hazard, aquatic toxicity, exposure, and risk among other factors. OPPT has computerized many of these methods and uses these to evaluate PMNs and existing chemicals where data are lacking. OPPT has over 20 years of experience in this area.

P2 Framework

The P2 Framework is a compilation of some of OPPT's most important methods for assessing hazard and risk when chemical specific data are lacking. This **P2 Framework Manual** describes each methodology contained in the P2 Framework and how the predictions generated can be used in decision making. This document also includes case studies showing how the methods can be used collectively to answer complicated risk assessment questions and identify P2 opportunities. The P2 Framework can provide important risk-related information that may not be available elsewhere. The purpose of the P2 Framework is to help identify pollution prevention opportunities by providing information that can inform decision making and help promote the design, development and application of safer chemicals and processes.

Risk Information Improves Decision Making

P2 Framework Methods Provide Screening Level Risk-Related Information

Most methods presented in OPPT's P2 Framework deal with two steps of the risk assessment process: hazard identification and exposure assessment. Ideally, information on the potential hazards posed by a chemical as well as exposure information will be available, but often this is not the case. Methods included in the P2 Framework are intended to provide screening level information to help in assessing potential risk posed by a chemical or group of chemicals.

What to Do When There Are No Data

The methods are intended to be used when data are unavailable or to supplement available data. These methods are generally computer models that assess a particular aspect of a chemical's possible impact on humans or the environment. For example, one model estimates toxicity to fish, aquatic invertebrates, and algae. This is important information if the chemical is or will be discharged to streams during manufacture, processing, use, or disposal. The OncoLogic model estimates the likelihood that a chemical would cause cancer in humans. Other models estimate potential exposures to a chemical in consumer products. Models are also presented for estimating properties such as vapor pressure and water solubility, which are important for projecting the nature, magnitude, and duration of exposure.

P2 Framework Outreach

OPPT wanted to learn if its SAR techniques could be transferred to industry and if these methods could be used early in R&D to evaluate PMN product alternatives based on risk. OPPT integrated these methods into a program called the Pollution Prevention Framework (P2 Framework), a science-based analytical framework for identifying safer new chemicals. OPPT developed P2 Partnerships with many industry sectors to help them explore the application of the P2 Framework methods to their chemicals of interest.

Summary of Kodak and PPG XL Projects

OPPT's outreach efforts to industry on the P2 Framework have been highly successful and formed the basis of two Project XLs with Kodak and PPG Industries. PPG and Kodak facilities are using the P2 Framework to screen all materials being considered for submission to EPA as new chemicals. Both companies will use the P2 Framework during the early stages of product development, allowing them to improve the environmental performance of products while reducing costs, saving time, enhancing competitive advantage and decreasing potential liability. Under the XL project, PPG verified the accuracy of the P2 Framework by comparing actual toxicity studies on 38 polymers with estimates from the P2 Framework with agreement between the two being 87- 90%. Kodak conducted an analysis of the economic and business benefits of application of the P2 Framework, and found that using the P2 Framework helped identify environmentally preferable products, lowered product development costs, reduced time to market and lowered full-scale manufacturing costs.

These Methods Provide Information in Four Areas

The P2 Framework models provide information in the following areas:

Physical/Chemical Properties
- Melting point
- Boiling point
- Vapor pressure
- Water solubility
- Henry's law constant
- Soil organic carbon adsorption

Hazard to Humans and the Environment
- Carcinogenicity potential
- Aquatic toxicity
- Non-cancer human health effects

Chemical Fate in the Environment
- Atmospheric oxidation potential
- Hydrolysis
- Biodegradation
- Bioconcentration and bioaccumulation
- Percent removal in wastewater treatment
- Percent in each media
- Persistence

Exposure and/or Risk
- Consumer dermal exposure
- Consumer inhalation exposure
- CC exceedences from discharges to surface water
- Workplace releases and exposures

The P2 Framework is set of screening-level methodologies that can be used when chemical-specific data are lacking. **If data are available for a given endpoint from a well conducted test, they should be used instead of data generated by the P2 Framework models or similar screening-level models.** Some methods included in the P2 Framework provide quantitative estimates (e.g., methods to estimate aquatic toxicity), while others, such as the OncoLogic model, provide qualitative hazard estimates. The computerized models in the P2 Framework do not address all human health effects. For this reason EPA has included a protocol that may be useful for screening chemicals for non-cancer human health effects.

Sustainable Futures Initiative – Regulatory Relief for Low Hazard/Low Risk New Chemical Substances

Sustainable Futures Initiative

Sustainable Futures (www.epa.gov/opptintr/newchems/sustainablefutures.htm) is the programmatic structure OPPT developed to scale-up the P2 Framework-based Kodak and PPG XLs (http://www.epa.gov/projectxl/), and is designed to help industry develop new chemicals that are sustainable economically and environmentally. OPPT published a Federal Register notice announcing Sustainable Futures on December 11, 2002. The FR Notice is available at www.epa.gov/fedrgstr/EPA-TOX/2002/December/Day-11/t31243.pdf. Sustainable Futures offers industry an integrated path to safer chemicals, this path includes: (1) comprehensive P2 Framework training, (2) specialized technical assistance within each industry sector, and (3) a Small Business Assistance Program, and strong incentives.

Incentives

OPPT is offering regulatory flexibility to companies that participate in Sustainable Futures, allowing qualifying low hazard/low risk chemicals to be manufactured in 45 days, rather than the current 90-day structure. This is a powerful incentive for many companies. In addition to getting to market sooner, regulatory uncertainty is greatly reduced because the P2 Framework helps anticipate, and engineer away from, chemicals of concern. This is P2 in it purest form. In addition, use of the P2 Framework reduces product development and manufacturing costs.

What Must Submitters Do to Qualify for Expedited PMN Review?

In order to qualify for this pilot project, and associated expedited review, companies subject to TSCA section 5 reporting requirements must demonstrate experience and competence with the P2 Framework or other scientifically acceptable approaches to chemical risk screening. In order to do this, companies will need to:

1. Take training in the use of risk screening models such as the P2 Framework and PBT Profiler. EPA sponsored training is listed at www.epa.gov/opptintr/newchems/sustainablefutures.htm
2. Apply hazard and exposure screening tools and demonstrate to EPA that this information has been used to inform decision making to select safer new chemical alternatives to submit as new chemical notifications (and, where appropriate, to identify opportunities to eliminate or control exposures through process controls); and
3. Submit 5-10 successful (i.e., not regulated by EPA) PMNs or PMN exemption notices which have been developed using chemical hazard and exposure screening tools. These submissions should also include documentation of chemicals evaluated, models used, endpoints on which decisions were based, and the submitter's perspectives on the extent to which the screening tools provided useful information to compare alternatives and select safer chemicals.

The Risk Standard Is Not Lowered

OPPT will continue to conduct an independent risk evaluation of each PMN submitted, and those that EPA finds to be low hazard/low risk qualify for relief. EPA makes this determination in the first 30 days of the 90-day review period. Chemicals that do not make the low hazard/low risk cut in the first 30 days won't qualify for relief. As a result, there will be no lowering of the risk standard.

Win-Win-Win

Under Sustainable Futures industry wins by getting to market sooner, reducing regulatory uncertainty, and lowering development/production costs. The environment wins because inherently safer chemicals and processes are commercialized. EPA wins by advancing key P2 and risk reduction goals and objectives.

P2 Framework Models

Model	Input	Output
Models to Estimate Physical / Chemical Properties		
MPBPVP™	CAS RN or Chem. Str. in SMILES	MP, BP, VP
WSKOWWIN™	CAS RN or Chem. Str. in SMILES	Water solubility from log KOW
KOWWIN™	CAS RN or Chem. Str. in SMILES	Octanol / water partition coefficient
HENRYWIN™	CAS RN or Chem. Str. in SMILES	Henry's law constant: VP/WS
PCKOCWIN™	CAS RN or Chem. Str. in SMILES	Soil organic carbon partition coefficient
Models to Estimate Chemical Fate in the Environment		
AOPWIN™	CAS RN or Chem. Str. in SMILES	Atmospheric oxidation potential
HYDROWIN™	CAS RN or Chem. Str. in SMILES	Hydrolysis rate
BIOWIN™	CAS RN or Chem. Str. in SMILES	Biodegradation potential
BCFWIN™	CAS RN or Chem. Str. in SMILES	Bioconcentration factor
STPWIN™	CAS RN or Chem. Str. in SMILES	Percent removal in POTW
LEV3EPI™	CAS RN or Chem. Str. in SMILES	Percent in each medium
Models to Estimate Hazards to Humans and the Environment		
OncoLogic	Chemical structure	Cancer hazard potential
ECOSAR	CAS RN or Chemical Structure in SMILES, if available measured WS, LogKow, MP	Acute and Chronic toxicity to fish, invertebrates, algae, SAR chemical class
PBT Profiler	CAS No. or Chemical structure drawn or in SMILES	Persistence: media half-lifes and percent in each medium; Bioaccumulation: fish BCF; Toxicity: fish chronic toxicity and identification of structures known to have human health concerns.
Models to Estimate Exposure and / or Risk		
E-FAST	Physical / chemical properties, fate properties, release amounts, release medium, release location, aquatic concentration of concern, NPDES number	Surface water ingestion, fish ingestion, ground water ingestion, ambient air inhalation, indoor air inhalation, dermal exposure, exposure/risk to aquatic environment
ChemSTEER	Production or assessed volume (kg chemical per year); chemical properties and workplace mass balance (when known); uses and workplaces to be assessed; % volume to each workplace; sources and activities with chemical releases and worker exposures	Media of release; number of sites; days of release per medium (days/ site-year); daily & annual release rates (kg/site-day & kg/year – all sites); Worker inhalation & dermal doses (mg/day &mg/kg/day) ; numbers of workers exposed

What is Required to Use the P2 Framework Models?

Essential Information

All of the tools require minimal, but important information. For example, physical and chemical properties such as molecular weight are important. Other models require the user to input the amount of chemical likely to be discharged to a stream or river. The table on the following page summarizes the required input information as well as the output data for each model.

Knowledge or Expertise Required

Knowledge needed will vary depending on the application. For example, the models KOWWIN and PCKOCWIN only require chemical structure or CAS Number; however, ECOSAR and OncoLogic require that the user have a good understanding of organic chemistry. The Screening for Non-cancer Human Health Effects protocol should be by an experienced human health toxicologist. User's Guides and technical assistance are available to help when you are uncertain how to proceed.

Computer Requirements

These models are designed to run on IBM compatible personal computers. The specific computer requirements (memory and disk size) necessary to run each of these models vary and are provided on the following page.

Model Availability

Models to Estimate Physical/Chemical Properties of Chemicals:
MPBPVP™, WSKOWWIN™, KOWWIN™, HENRYWIN™ methods, incorporated into the EPI Suite™, were developed by Syracuse Research Corporation (SRC) for US EPA, OPPT and can be downloaded from www.epa.gov/opptintr/exposure/docs/EPI Suitedl.htm

Models to Estimate Chemical Fate in the Environment:
AOPWIN™, HYDROWIN™, BIOWIN™, PCKOCWIN™, BCFWIN™, STPWIN™, LEV3EPI™ incorporated into the EPI Suite™, were developed by SRC for US EPA, OPPT and can be downloaded from www.epa.gov/opptintr/exposure/docs/EPI Suitedl.htm
The LEV3EPI™ fugacity model is based on Level III Fugacity model developed by Don Mackay of Trent University (www.trentu.ca/cemc/VBL3D.html). LEV3EPI has been incorporated into the EPI Suite™ and can be downloaded from the Internet at. www.epa.gov/opptintr/exposure/docs/EPI Suitedl.htm.

Models to Estimate Hazard to Humans and the Environment:
OncoLogic, developed by LogiChem under a cooperative agreement with USEPA, OPPT in support of Sec. 5 of TSCA, can be obtained by contacting: Marilyn S. Arnott, Ph.D., LogiChem, Inc., PO Box 622, Narberth, PA 19072, Email: marnott@ptdprolog.net
ECOSAR can be downloaded from the Internet at: www.epa.gov/oppt/newchems/21ecosar.htm or by contacting Vince Nabholz, EPA, OPPT at nabholz.joe@epa.gov

Model to Estimate Persistence, Bioaccumulation, and Toxicity
The PBT Profiler screening model was developed by SRC for OPPT to help users prioritize chemicals based on their potential to persist, bioaccumulate, and be toxic. The PBT Profiler can be accessed on the Internet at www.pbtprofiler.net.

Modes to Estimate Exposure and/or Risk:
The E-FAST Model and documentation manual can be downloaded at no cost from EPA's Internet site at: www.epa.gov/opptintr/exposure/docs/efast.htm
ChemSTEER can be downloaded at no cost from EPA's Internet site at: www.epa.gov/opptintr/exposure/docs/chemsteer.htm

Computer Requirements

Computer Requirements

The P2 Framework models are designed to run on IBM compatible personal computers. The specific computer requirements (memory and disk size) necessary to run each of these models vary and are provided below.

EPI Suite™ which includes MPBPVP™, WSKOWWIN™, KOWWIN™, HENRYWIN™, AOPWIN™, WVOLWIN™, HYDROWIN™, BIOWIN™, PCKOCWIN™, BCFWIN™, STPWIN™, and LEV3EPI™, requires:

- IBM-compatible PC with Microsoft Windows 3.1, 95, 98, 2000 and Windows NT
- 10 MB of hard disk space
- SMILECAS requires 10 MB of hard disk space
- LEV3EPI requires at least a 75MHz processor (adjustment of screen resolution may be necessary)

OncoLogic

- 386 PC with MS-DOS 5.0 or later,
- 570K of conventional RAM
- 60 megabytes of hard disk space
- A disk cache will significantly improve performance

ECOSAR

- IBM-compatible PC with a 640-KB memory
- 512-550 KB of free memory
- 80386 or 80286 processor
- MS Windows 3.1, 95, 98, or NT
- Expanded memory and disk cache will improve performance
- At least 51 file handlers specified in the CONFIG.SIS file

PBT Profiler

- Java-enabled web browser that is set to accept cookies

E-FAST

- IBM-compatible PC with a 640-KB memory
- 512-550 KB of free memory
- 80386 or 80286 processor
- MS Windows 3.1, 95, 98, or NT
- At least 51 file handlers specified in your CONFIG.SIS file
- An expanded memory and disk cache will improve performance

ChemSTEER

- IBM-compatible PC Pentium or higher processor (500 MHz or faster recommended)
- Monitor with 800 x 600 resolution or higher
- Windows 95 or higher
- 64 megabytes of memory
- 30 megabytes of hard disk space (installed files); 25 MB (installation file can be deleted following installation)

About This Document

Contents of This Document

This manual explains the models used by OPPT to screen potential exposures and risks posed by chemicals. Each model answers important questions about a chemical's potential impact on humans or the environment. The models are described in this document by briefly detailing the important information they provide. Flow diagrams presenting step-by-step use of some of the more complex models are also included. In addition, a series of structured examples (case studies) are provided to show how the models can answer specific environmental questions and how the models can be used in combination to answer complicated exposure/risk-related questions.

We believe this information will be useful to you. The manual provides some information on how to use the models. However, we recognize that you may still have questions after you read this material. Technical assistance is available from OPPT to answer those questions.

Users of This Document

You are reading this manual because you are interested in opportunities to prevent pollution. These opportunities may also decrease costs to your company or organization. As you read, please keep in mind that this version of the P2 Framework is the first step in an evolving process. All comments and suggestions for improvement are welcome. Please direct comments to:

Maggie Wilson, EPA, OPPT
Phone: 202-564-8924
Email: wilson.maggie@epa.gov

How This Document Is Organized

This document presents brief overviews of each model. Each overview provides enough information to successfully run each model. More detailed information on each model is provided in the User's Guide or supplemental documentation for that model.

A glossary of relevant terms is also included. Appendices include (1) Case Studies which illustrate how the models can be used in combination to answer complicated risk-related questions; (2) Data Sources to search for measured data; (3) and Summary of Writing SMILES notation.

P2 Framework Models

The models included in this manual are listed below, and are presented in the illustration on the following page. The illustration can be used as an informal "road map" to approximate the endpoints the model addresses and help decide which models you might wish to use.

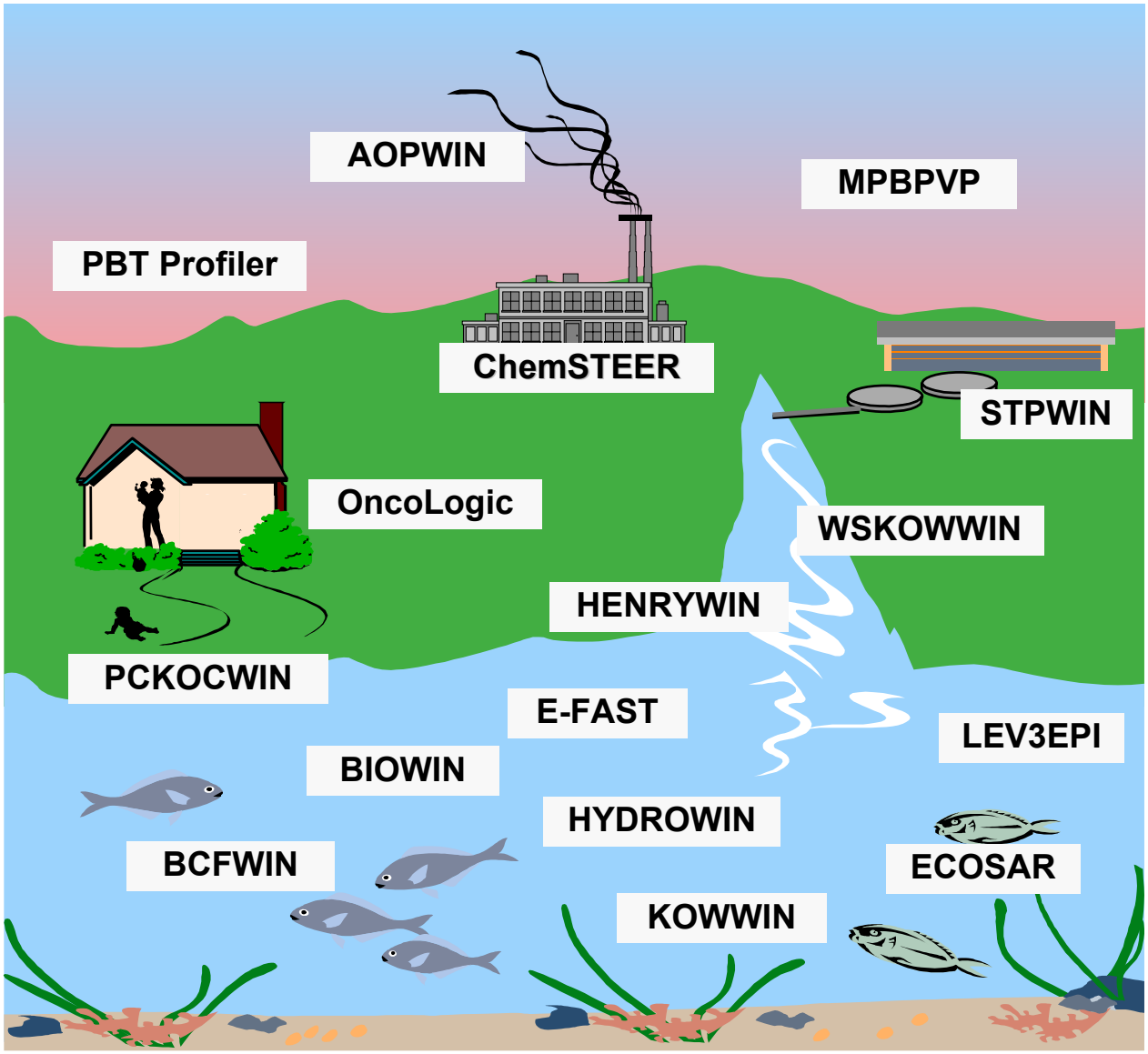
PHYSICAL/CHEMICAL PROPERTY MODELS:
MPBPVP™, WSKOWIN™, KOWWIN™, HENRYWIN™

FATE MODELS:
AOPWIN™, HYDROWIN™, BIOWIN™, PCKOCWIN™, BCFWIN™, STPWIN™, LEV3EPI™

HAZARD MODELS:
OncoLogic, ECOSAR

P, B, T POTENTIAL:
The PBT Profiler

EXPOSURE and/or RISK MODELS:
E-FAST, ChemSTEER



EPI Suite™ and SMILES

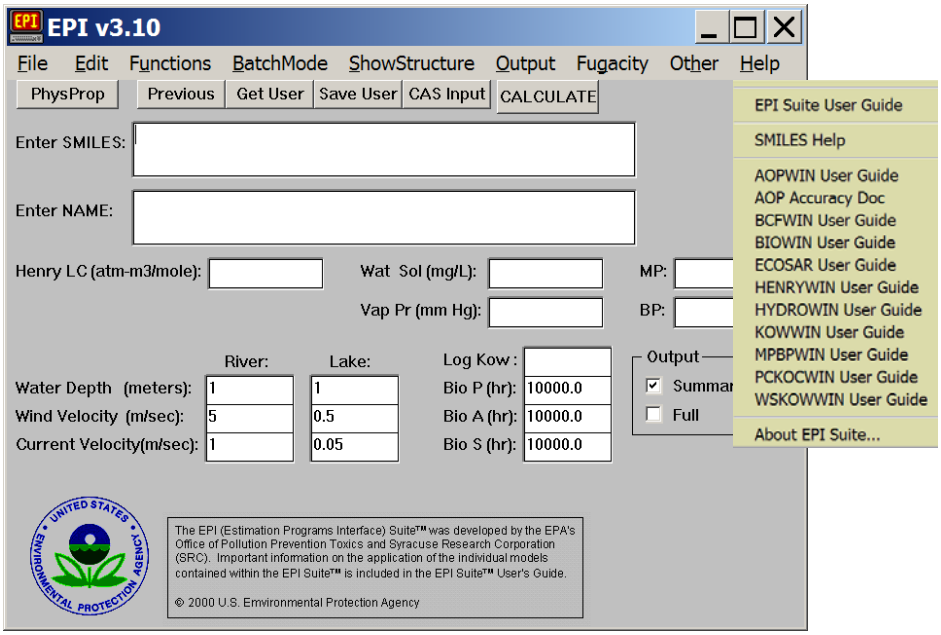
What Is EPI Suite™?

Estimations Programs Interface for Windows - EPI Suite™ - provides a quick and easy way to run the estimation programs, listed below, from a single entry for a single chemical. EPI Suite™ can sequentially run: AOPWIN™, BCFWIN™, BIOWIN™, ECOSAR, HENRYWIN™, HYDROWIN™, KOWWIN™, LEV3EPI™, MPBPVP™, PCKOCWIN™, STPWIN™ and WSKOWWIN™. The chemical structure or CAS Number is entered only once, and EPI Suite™ executes all of the programs in sequence and captures their output. Any of the estimation programs may be run separately. EPI Suite™ can be operated in a "Batch Mode" so that many structures (as SMILES strings, CAS RNs, or MDL files) can be entered and run at one time. The EPI Suite™ Programs also can input chemical structure formats generated by other computer programs. These importable formats include:

- Alchemy III MOL files
- Beilstein ROSDAL files
- BioCAD Catalyst TPL files
- ChemDraw files
- ChemDraw Connection Tables
- HyperChem HIN files
- MDL ISIS SKC files
- MDL MOL files
- Molecular Presentation Graphics (MPG) files
- PCModel files
- Softshell SCF files
- Tripos Sybyl Line Notation
- Tripos SYBYL MOL2 files

EPI Suite™ Data Entry

To the right is the EPI Suite™ data entry page. A chemical is entered only once and EPI will run each of the estimation programs, listed above, and provide results from each program. Chemical structure can be entered using CAS RN, Smiles string, or imported from a chemical draw Program. Many good draw programs are available, such as ISIS Draw, which is available at no cost from MDL at www.mdli.com



The User's Guide for each model is available in the Help screens.

What Is SMILES?

SMILES is "Simplified Molecular Input Line Entry System," which translates a chemical's structure into a string of symbols that is easily understood by computer software. You can learn to write SMILES notations, as described in Appendix C. For all EPI Suite™ estimation programs, enter only the SMILES notation for the chemical, and the program provides the estimation you need.

Writing SMILES Notations

The SMILES notation system was designed by chemists for computer use (Weininger, 1988. J. Chem. Inf. Comput. Sci. 28: 31-6). SMILES notations depict the molecular structure of a chemical as a 2-dimensional picture. Learning to write a SMILES notation is not difficult, but it can be tricky. The same 3-dimensional structure can be written correctly using many different SMILES notations.

A summary of directions for writing SMILES notations is included in Appendix C of this document. Complete directions for writing SMILES notations are included in the EPI Suite™ User's Guide, and the Help files in each EPI Suite™ and the ECOSAR model include examples of SMILES notations.